RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	naproxen and esomeprazole magnesium
Policy Number:	RxA.552
Drug(s) Applied:	Vimovo®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Naproxen and esomeprazole magnesium (Vimovo®) is a combination of a nonsteroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor (PPI).

It is indicated in adult and adolescent patients 12 years of age and older weighing at least 38 kg, requiring naproxen for symptomatic relief of arthritis and esomeprazole magnesium to decrease the risk for developing naproxen-associated gastric ulcers.

The naproxen component of Vimovo® is indicated for relief of signs and symptoms of:
- Osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in adults.
- Juvenile idiopathic arthritis (JIA) in adolescent patients.

The esomeprazole magnesium component of Vimovo® is indicated to decrease the risk of developing naproxen-associated gastric ulcers.

Limitation(s) of use:
- Do not substitute Vimovo® with the single-ingredient products of naproxen and esomeprazole magnesium.
- Vimovo® is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared to absorption from other naproxen-containing products.
- Controlled studies do not extend beyond 6 months.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
naproxen and esomeprazole (Vimovo®)	Rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis	One tablet PO BID of either 375 mg naproxen/20 mg esomeprazole or 500 mg naproxen/20 mg esomeprazole	1000 mg naproxen/40mg esomeprazole per day
	Juvenile idiopathic arthritis in adolescent patients 12 years of age and older and weighing at least 38 kg	> 50 kg: One tablet PO BID of either 375 mg naproxen/20 mg esomeprazole or 500 mg	> 50 kg: 1000 mg naproxen/40mg esomeprazole per day

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
		naproxen/20 mg esomeprazole	
		38 to < 50 kg: 375 mg naproxen/20 mg esomeprazole PO BID	38 to 50 kg: 750 mg naproxen/40 mg esomeprazole per day

Dosage Forms

- Delayed-release tablets (enteric-coated naproxen/immediate-release esomeprazole): 375 mg/20 mg and 500 mg/20 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. All FDA Approved Indications (must meet all):

1. Prescribed to decrease the risk of developing NSAID-induced gastric ulcers in patients with rheumatoid arthritis, JIA, osteoarthritis, or ankylosing spondylitis;
2. Age ≥ 12 years;
3. Failure of three PPIs (e.g., omeprazole, pantoprazole, lansoprazole) in combination with three different NSAIDs, unless contraindicated or clinically significant adverse effects are experienced;
4. Medical justification supports inability to use the individual components (i.e., esomeprazole* and naproxen) concurrently (e.g., contraindications to the excipients of all brand and generic products); *Prior authorization may be required for esomeprazole.
5. Dose does not exceed 1000 mg naproxen/40mg esomeprazole per day (2 tablets per day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All FDA Approved Indications (must meet all):

1. Member is currently receiving the medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 1000 mg naproxen/40mg esomeprazole per day (2 tablets per day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NSAID: nonsteroidal anti-inflammatory
GI: gastrointestinal drug
JIA: juvenile idiopathic arthritis
PPI: proton pump inhibitor

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
PPIs		
lansoprazole (Prevacid®)	NSAID-induced ulcer prophylaxis: 15 mg PO once daily NSAID-associated gastric ulcer (healing): 30 mg PO once daily	30 mg/day (for most indications)
omeprazole (Prilosec®)	NSAID-induced ulcer prophylaxis†: 20 mg PO once daily	40 mg/day (for most indications)
pantoprazole (Protonix®)	NSAID-induced ulcer prophylaxis†: 40 mg PO once daily	40 mg/day (for most GERD indications)
NSAIDs		
diclofenac (Voltaren®)	Osteoarthritis: 50 mg PO BID-TID or 75 mg PO BID Rheumatoid arthritis: 50 mg PO TID-QID, or 75 mg PO BID Ankylosing spondylitis: 25 mg PO QID with an additional 25 mg dose at bedtime	Osteoarthritis: 150 mg/day Rheumatoid arthritis: 200 mg/day Ankylosing spondylitis 125 mg/day
etodolac (Lodine®)	Osteoarthritis or rheumatoid arthritis: 400–500 mg PO BID	1200 mg/day
fenoprofen (Nalfon®)	400--600 mg PO TID-QID	3200 mg/day
ibuprofen (Motrin®)	400–800 mg PO TID-QID	3200 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
indomethacin (Indocin®)	25 PO BID-TID	200 mg/day
	50 mg PO QID or 75 mg PO TID	300mg/day
meloxicam (Mobic®)	7.5 mg–15 mg PO once daily	15 mg/day
naproxen (Naprosyn®)	250–500 mg PO BID	1500 mg/day
naproxen sodium (Anaprox® DS)	275–550 mg PO BID	1650 mg/day
oxaprozin (Daypro®)	600–1200 mg PO once daily	1800 mg/day
piroxicam (Feldene®)	10–20 mg PO once daily	20 mg/day
salsalate	1500 mg PO BID or 1,000 mg PO TID	3000 mg/day
	150 mg-200 mg PO BID	400 mg/day
tolmetin	400–600 mg PO TID	1800 mg/day
meclofenamate	50–100 mg PO Q4-6hr	400 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic. †Off-label indication

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to naproxen, esomeprazole magnesium, substituted benzimidazoles, or to any components of the drug product including omeprazole;
  - history of asthma, urticaria, or other allergic-type reactions to aspirin or other NSAIDs;
  - in the setting of coronary artery bypass graft (CABG) surgery;
  - concurrent use of rilpivirine-containing products.

- Boxed Warning(s):
  - NSAIDs cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal;
  - NSAIDs, including naproxen, cause an increased risk of serious GI adverse events including bleeding, ulceration, and perforation of the stomach or intestines.

APPENDIX D: General Information

- Vimovo delivers relief from OA/RA pain and inflammation with at least 70% lower risk of developing stomach ulcers than patients on naproxen alone.
- The most common side effects of VIMOVO are inflammation of the lining of the stomach and diarrhea.

References

1. Vimovo Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; July 2019. Available at: www.vimovo.com. Accessed September 25, 2020.
2. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed September 25, 2020.

3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed September 25, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title table was updated as "naproxen and esomeprazole magnesium" 2. Line of business policies applies to All lines of business. 3. Dosing Information updated. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by Rxadvance." 5. Appendix B updated. 6. Appendix D updated with common side-effects included. 7. References were reviewed and updated.	09/25/2020	12/07/2020